Docket No 63419 (52171)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Wolfgang Richter, Lutz Weber

Application No.: 10/535,474 | Confirmation No.: 4298

Filed: November 28, 2003 | Art Unit: 1626

For: THIA-EPOTHILONE DERIVATIVES FOR THE TREATMENT OF CANCER | Examiner: Joseph R. Kosack

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF WOLFGANG RITCHER,PH.D, UNDER 37 C.F.R. § 1.132

I, Dr. Wolfgang Richter, declare as follows:

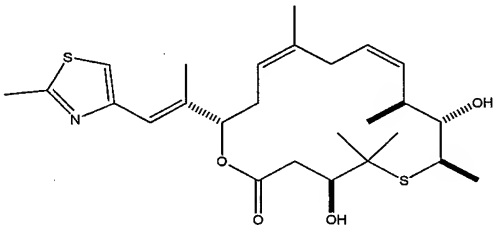
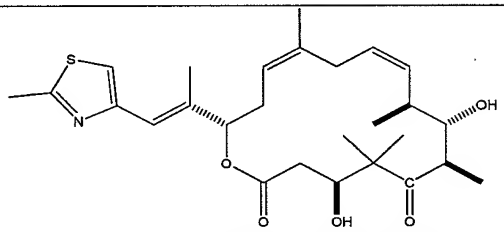
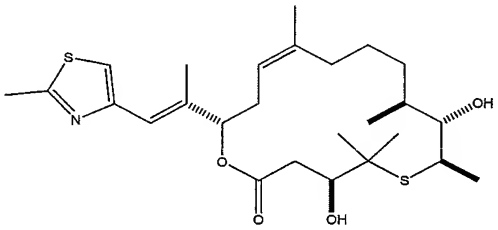
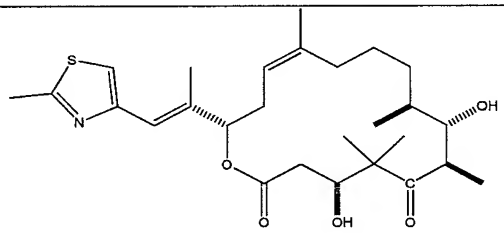
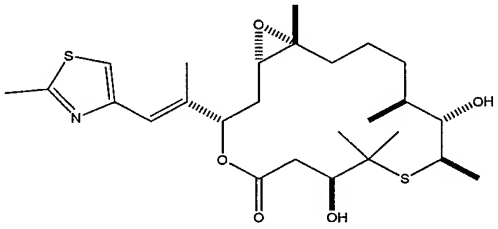
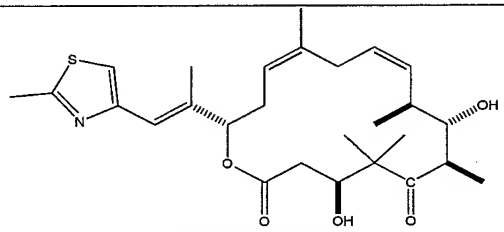
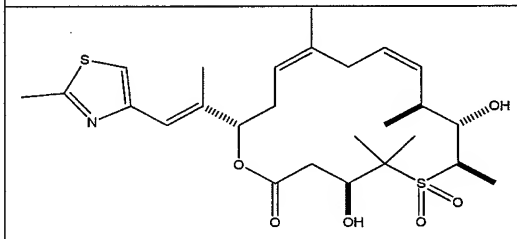
1. I am managing Director of R&D Biopharmaceuticals GmbH, Munich , Germany. My field of research and expertise is in the area of organic and medicinal chemistry. I am an inventor of the above-referenced application (the "Application").

2. The following experimental data was obtained in accordance with the following citations: J.D. White et al., J. Am. Chem. Soc. 2001, 123, 5407-5413 ("Document A1"). K.H. Altmann, Mini Reviews in Medicinal Chemistry 2003, 3, 149-158 ("Document A2").

3. The following experimental data exemplifies that epothilone derivatives according to the present invention having either a sulfide or sulfone function at the 5-position are active against the human breast cancer line MCF-7 and/or human epidermoid cancer line kb-31 (see table 1 below, left column).

4. Also shown in the table below are corresponding known epothilone derivatives having a carbonyl function at the 5-position (see table 1 below, right column)

Table 1: IC_{50} values [nM] for growth inhibition of cancer cell lines MCF-7 and KB-31

Epothilone with S or SO2 at 5-position	IC_{50} (nM)	Epothilone with CO at 5-position	IC_{50} (nM)
	50-70 (MCF-7)	 *cis*-9,10-dehydroepothilone D	72 [1] (MCF-7)
	3-8 (MCF-7)	 Epothilone D	2.31 [1] (MCF-7)
	0.5-2 (MCF-7) 0.4-1.5 (KB-31)	 Epothilone B	0.29-0.42 [1,2] (MCF-7) 0.19-1.2 [2] (KB-31)
	1.2-2.5 (MCF-7)		

[1] Document A1 (Page 5413, table 1)

[2] Document A2 (Page 151, table 1; Page 152, table 3; Page 154, table 4)

5. The experimental data presented herein demonstrates that replacing the carbonyl function at the 5-position of an epothilone derivative by a sulfide or a sulfone function results in an epothilone derivatives having a similar activity against certain cancer cell lines.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Date: September 8th, 2008

Respectfully Submitted,

By: Wolfgang Ritcher